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The role of Screening for Herpes Simplex Virus in Candidates of Renal Transplantation

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Background: Herpes Simplex Virus (HSV) infection in immunocompromised hosts like kidney transplant patients causes more morbidity and mortality than the general population.
Objectives: The aim of this study was to evaluate the role of screening for HSV in donors and recipients of kidney transplantation.
Materials and Methods: From October 2012 to November 2013, this cross sectional study was conducted on donors and recipients who were referred to our kidney transplant center in Ahvaz city, Iran. A standardized questionnaire was used to collect social and demographic data. The patients and donors were screened for HSV IgG and IgM antibodies by direct fluorescent antibody (DFA).Other routine pretransplant laboratory studies were also performed.
Results: Overall 37 people (22 donors, 20 males and 2 females with mean age of 30 ± 5 years; 15 recipients, eight males and seven females with mean age of 45 ± 6 years) were enrolled in this study. All of the recipients were on hemodialysis. The markers of HBV and HCV infection were negative in 100% of recipients and donors. Herpes Simplex Virus (HSV) IgG antibody was positive in 93.33% of recipients (n = 14) and 77.27% of donors (n = 17). Herpes Simplex Virus (HAV) IgM antibody was positive in 33.33% of recipients (n = 5) and 13.63% of donors (n = 3).
Conclusions: Herpes Simplex Virus is a common infection in donor and recipient candidates for kidney transplantation in Khuzestan province of Iran, and it seems that we need to perform screening for this infection to avoid kidney donation from seropositive donors to seronegative recipients.

Keywords: Kidney Transplantation; Simplexvirus; Antibodies

1. Background

Infections are a major cause of morbidity and mortality among solid organ transplant patients as more than 80% of these patients suffer at least one episode of infection during the first year after transplantation. The concurrent administration of immunosuppressive drugs to prevent acute allograft rejection further increases the risk of morbidity and mortality among these patients (1, 2). Although cytomegalovirus is the most important, and one of the most common infections seen in renal transplant recipients, numerous other viruses have also affected outcomes (3-11). Herpes simplex virus (HSV) is an alpha herpes virus with a double stranded DNA core. According to previous studies, the seroprevalence of HSV in the adult population is as high as 60% (12, 13). Therefore, donor and recipient candidates for kidney transplantation are also at risk of this infection. Although, there are many studies about the prevalence of HSV infection in the general population or transplant candidates in developed countries, yet only a few studies have been done in developing countries regarding this issue.

2. Objectives

The aim of this study was to evaluate the role of screening and the prevalence of HSV infection in donor and recipient candidates for kidney transplantation in Ahvaz city of Iran.

3. Materials and Methods

In this cross sectional study, from October 2012 to November 2013, we investigated all candidates for receiving renal allograft and living donors who had referred to our kidney transplant center before transplantation. The study was approved by the chronic renal failure research center of Ahvaz Jundishapur University of Medical Sciences.

A standardized questionnaire was used to collect sociodemographic data (for donors and recipients) including causes of end stage renal disease (ESRD), date of onset and length of time before receiving renal replacement therapy and history of a kidney transplantation (for recipients).

Blood samples were taken from recipients and donors

to test for IgG and IgM anti-HSV antibodies (Trinity Biotech, New York, USA). The levels of antibodies were determined by using a commercially available direct fluorescent antibody (DFA) method. The recipients and donors were also screened for human immunodeficiency virus (HIV) (Pishtaz Teb Zamen, Tehran, Iran), HBsAg and hepatitis C antibody (anti-HCV) (Pasto kit, Pasteur Institute, Iran) by using the sensitive enzyme-linked immunosorbent assay (ELISA). All samples were also tested for liver function including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels by a colorimetric method. Liver function tests including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were also determined by a colorimetric method. Medical laboratory tests were performed for the recipients and donors free of charge by the hospital.

3.1. Hemodialysis Methods

Hemodialysis (HD) was performed during six to 16 hours, two, three or four times a week according to clinical grounds. The rate of ultrafiltration rate during each hemodialysis (HD) session was also determined by the nephrologist. We used Fresenius machines, synthetic (polysulfone) dialyzer membranes and bicarbonate-buffered dialysate for our patients.

3. 2. Statistical Analysis

At the end of the study, we performed statistical analysis using the statistical package for social sciences (SPSS) software version 15. Results are expressed as mean ± SD. Prevalence rates and 95% confidence intervals (CI 95%) were calculated. Chi-square tests were performed to evaluate the distribution of variables associated with herpes simplex virus infection. A P value of less than 0.05 was considered statistically significant.

4. Results

Overall, 37 candidates for kidney transplantation were enrolled in this study. There were 22 candidates for kidney donation with mean age of 30 ± 5 years with most being males; 20 males (90.90%) and two females (09.09%). Our recipients included 15 dialysis patients; eight males (53.33%) and seven females (46.66%) with mean age of 45 ± 6 years.

The minimum and maximum ages of the candidates were 21 and 60 years for donors and 19 and 66 years for recipients, respectively. All of our recipients were on maintenance intermittent hemodialysis. Herpes simplex virus IgG antibody was positive in 93.33% of recipients (n = 14) and 77.27% of donors (n = 17). Although the prevalence of positivity for HSV IgG antibody was higher in recipients, there was no statistically significant difference between the two groups (P = 0 .33). Herpes simplex virus IgM antibody was positive in 33.33% of recipients (n = 5) and 13.63% of donors (n = 3) and there was no statistically significant difference between the two groups (P = 0.15). The liver function tests indicated that AST and ALT were at normal ranges in both recipients and donors. The markers of HBV and HCV infection were also negative in all recipients and donors.

5. Discussion

Herpes simplex virus infection is a well-known opportunistic pathogen among immunocompromised patients including kidney transplant recipients. This infection is usually caused by reactivation of latent virus among these patients; however, it has also been recognized as a potential donor-to-host transmission infection after transplantation. In the absence of prophylaxis, HSV may be seen early, even during the first post transplant month (14-16). Although it usually presents oral or genital lesions, it can also be a life threatening disease with high morbidity and mortality among infected patients (14, 15). For example in some instances, it can cause life threatening diseases including esophagitis, hepatitis, encephalitis or pneumonitis. It may be difficult to differentiate between an infection acquired from the allograft, and an infection due to reactivation of latent disease in the recipient (14).

The results of our study show that, the prevalence of HSV IgG antibody and therefore exposure to the HSV infection in candidates for kidney transplantation in Khuzestan province of Iran, is high and almost all of the recipients (93.33%) and most of the donors (77.27%) had the HSV IgG antibody before transplantation. Similar to the result of our study, the incidence of HSV in renal transplant recipients was also high and estimated to be approximately 53% (15). Other studies have reported that HSV can cause pneumonia, which may lead to a mortality rate of up to 75% despite treatment with acyclovir (16, 17). Walker et al. in a prospective study of HSV disease in renal transplant recipients, reported that HSV infection was diagnosed in about 52% of the studied patients (18).

Regarding the prevalence of HSV infection among donors and recipients, due to probability transmission of infection from seropositive donors to seronegative recipients, and the potential of reactivation of the latent virus among recipients, it is recommended for recipients and donors of kidney transplantation to be routinely tested for IgM and IgG anti–HSV antibodies before transplantation while recipients should be followed to monitor for reactivation of latent virus following immunosuppressive treatments (14, 15, 19, 20).

In addition, post-transplant prophylaxis against reactivation of HSV is also recommended to prevent severe recurrences of this infection. In patients who need cytomegalovirus (CMV) prophylaxis, ganciclovir is adequate against both CMV and HSV infections. Among kidney transplant patients who do not require CMV prophylaxis, valacyclovir or acyclovir should be administered for approximately one to three months post transplantation

(21-26). Herpes simplex virus infection is a well-known opportunistic pathogen among kidney transplant recipients. It may become a life threatening disease among these patients. This infection is usually caused by reactivation of latent virus or by transmission from seropositive donors to seronegative recipients.

The results of our study show that, almost all of the recipients and most of the donors for kidney transplantation in Khuzestan province Iran had HSV IgG antibody and exposure to the infection. The incidence of HSV infection in other countries is also high and therefore it is recommended that both the recipients and donors for kidney transplantation should be routinely tested for IgM and IgG anti–HSV antibodies before transplantation while recipients should be monitored for reactivation of latent virus following immunosuppressive treatments.

References

1. Rubin RH. Infectious disease complications of renal transplantation. *Kidney Int.* 1993;**44**(1):221–36.
2. Jamil B, Nicholls K, Becker GJ, Walker RG. Impact of acute rejection therapy on infections and malignancies in renal transplant recipients. *Transplantation.* 1999;**68**(10):1597–603.
3. Kotton CN, Fishman JA. Viral infection in the renal transplant recipient. *J Am Soc Nephrol.* 2005;**16**(6):1758–74.
4. Smith SR, Butterly DW, Alexander BD, Greenberg A. Viral infections after renal transplantation. *Am J Kidney Dis.* 2001; **37**(4):659–76.
5. Fishman JA, Rubin RH. Infection in organ-transplant recipients. *N Engl J Med.* 1998;**338**(24):1741–51.
6. Beladi-Mousavi SS, Hayati F, Ghorbani A. Seroprevalence of cytomegalovirus antibody in renal transplant recipients and donors in Khuzestan Province, Iran. *Shiraz E-Med J.* 2010;**11**(4):203–8.
7. Seifollah Beladi Mousavi S, Faramarzi M. Do we Need to Screen Uremic Patients for Toxoplasmosis before Kidney Transplantation? *Shiraz E-Med J.* 2013;**14**(4).
8. Beladi-Mousavi SS, Hajiani E, Salehi-Behbehani SM. Hepatitis B Infection in ESRD Patients in Khuzestan Province, Iran. *Iran J Virol.* 2010;**4**(2):45–8.
9. BeladiMousavi SS, Hajiani E, Hayati F, Hashemi SJ, Shayesteh A, Salehi-Behbehani SM, et al. Epidemiology of Hepatitis C Virus Infection in ESRD Patients in Khuzestan Province, Iran. *Shiraz E-Med J.* 2012;**13**(3):135–40.
10. Beladi Mousavi SS, Motemednia F, Beladi Mousavi M. Epidemiology of hepatitis e virus infection in patients on chronic hemodialysis. *Jundishapur J Microbiol.* 2014;**7**(5).
11. Beladi Mousavi SS. Do we need to screen our patients for EBV IgG antibody before kidney transplantation? *Nephro Urol Mon.* 2011;**3**(2):122–4.
12. Crumpacker CS, Wadhwa S. Cytomegalovirus. In: Mandell GM, Bennett JE, Dolin R editors. *Principles and Practices of Infectious Diseases.* 4th ed. New York: Churchill Livingstone; 2005. pp. 1786–801.
13. Cowan FM, Copas A, Johnson AM, Ashley R, Corey L, Mindel A. Herpes simplex virus type 1 infection: a sexually transmitted infection of adolescence? *Sex Transm Infect.* 2002;**78**(5):346–8.
14. Green M, Avery R, Preiksaitis J. Guidelines for the prevention and management of infectious complications of solid organ transplantation. *Am J Transplant.* 2004;**4**(10).
15. Patel R, Paya CV. Infections in solid-organ transplant recipients. *Clin Microbiol Rev.* 1997;**10**(1):86–124.
16. De Biase L, Venditti M, Gallo P, Macchiarelli A, Tonelli E, Scibilia G, et al. Herpes simplex pneumonia in a heart transplant recipient. *Recenti Prog Med.* 1992;**83**(6):341–3.
17. Allen KA, Markin RS, Rennard SI, Shaw BJ, Thompson AB, Wood RP, et al. Bronchoalveolar lavage in liver transplant patients. *Acta Cytol.* 1989;**33**(4):539–43.
18. Walker DP, Longson M, Mallick NP, Johnson RW. A prospective study of cytomegalovirus and herpes simplex virus disease in renal transplant recipients. *J Clin Pathol.* 1982;**35**(11):1190–3.
19. Broyer M, Tete MJ, Guest G, Gagnadoux MF, Rouzioux C. Varicella and zoster in children after kidney transplantation: long-term results of vaccination. *Pediatrics.* 1997;**99**(1):35–9.
20. Olson AD, Shope TC, Flynn JT. Pretransplant varicella vaccination is cost-effective in pediatric renal transplantation. *Pediatr Transplant.* 2001;**5**(1):44–50.
21. Strippoli GF, Hodson EM, Jones C, Craig JC. Preemptive treatment for cytomegalovirus viremia to prevent cytomegalovirus disease in solid organ transplant recipients. *Transplantation.* 2006;**81**(2):139–45.
22. Kalil AC, Levitsky J, Lyden E, Stoner J, Freifeld AG. Meta-analysis: the efficacy of strategies to prevent organ disease by cytomegalovirus in solid organ transplant recipients. *Ann Intern Med.* 2005;**143**(12):870–80.
23. Hodson EM, Jones CA, Webster AC, Strippoli GF, Barclay PG, Kable K, et al. Antiviral medications to prevent cytomegalovirus disease and early death in recipients of solid-organ transplants: a systematic review of randomised controlled trials. *Lancet.* 2005;**365**(9477):2105–15.
24. Hart GD, Paya CV. Prophylaxis for CMV should now replace preemptive therapy in solid organ transplantation. *Rev Med Virol.* 2001;**11**(2):73–81.
25. Jassal SV, Roscoe JM, Zaltzman JS, Mazzulli T, Krajden M, Gadawski M, et al. Clinical practice guidelines: prevention of cytomegalovirus disease after renal transplantation. *J Am Soc Nephrol.* 1998;**9**(9):1697–708.
26. Burke G3, Kaufman DB, Millis JM, Gaber AO, Johnson CP, Sutherland DE, et al. Prospective, randomized trial of the effect of antibody induction in simultaneous pancreas and kidney transplantation: three-year results. *Transplantation.* 2004;**77**(8):1269–75.